TABLE III

VALUES FOR THE DEUTERIUM EVOLUTION REACTION FROM 1-HYDROXYISOBUTYL-1-*d* ISOBUTYL-1,1-d_2 PEROXIDES IN α-METHYLSTYRENE

Temp.,[a] °C.	$k \times 10^5$, sec.$^{-1}$ [b]	$k_D \times 10^5$, sec.$^{-1}$ [c]	k_H/k_D	A[d] $\times 10^{-7}$	ΔS^*[e]	ΔF^*[f]
(A)	1-Hydroxyisobutyl-1-*d* isobutyl-1,1-d_2 peroxide					
99.6	6.9	2.6	3.4	7.1	−24.6	30.0
109.8	18	4.8		6.5	−25.0	30.4
110.0	19	5.2	3.9[g]	5.5	−24.7	30.3
122.0	42	13.0	3.2[h]	7.6	−24.7	30.6

[a] See footnote *a*, Table I. [b] Observed rate constant for all reactions involved. [c] Rate constant for formation of deuterium. [d] Arrhenius frequency factor, sec.$^{-1}$; the Arrhenius energy of activation E_a was 21.4 kcal./mole. [e] Entropy of activation, cal./mole/degree; the enthalpy of activation, ΔH^*, was 20.8 kcal./mole. [f] Free energy of activation, kcal./mole. [g] Based upon average of two values for k_H and k_D. [h] Value for k_H obtained by extrapolation of data in ref. 1 = 4.2×10^{-4}.

sented in cases A and B. The isotope effect and the production of I *via* equilibrium 2 and RCHO formed from decomposition of IV, tend to enhance the discrepancies observed in this case more than the others.

Because of the contribution of each of these factors is not known, it is not feasible to make a quantitative evaluation of these data. In spite of these complications, however, these rate data are summarized in Table III, and should be useful in estimating a *minimum* isotope effect. The observed rate constant is corrected to give k_D by considering the yield of isotopic hydrogen, thus k_D contains a small k_H contribution.

The isotope effect is taken as the ratio of the rate constants for hydrogen[1] and deuterium evolution (k_H/k_D) assuming that compound A is 100% deuterated in the α-position. This ratio is seen to be 3.9 at 110°. If the labeled compound had been 100% deuterated in the α-position, a somewhat larger value undoubtedly would have been observed. Thus this is a minimum figure. The thermodynamic constants are also given in Table III. although their accuracy is not known because of the low yields of isotopic hydrogen. It is significant, however, that the value for the entropy of activation is clearly negative, about −25, similar to that obtained for the undeuterated compounds. The other thermodynamic values are also quite comparable to those for the undeuterated compounds.

The presence of this isotope effect and the negative entropy of activation are taken as evidence contrary to a radical cage process and in complete accord with the cyclic concerted mechanism previously postulated.[2]

Acknowledgment.—The authors wish to thank the National Science Foundation and Petroleum Research Board for financial support of this work and Dr. Harold Johnston and Dr. Russell Hardwick for valuable discussions throughout the course of this investigation.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN, BROOKLYN 1, N. Y.]

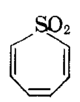
Reactions in Medium-sized Cyclic Sulfides[1]

BY C. G. OVERBERGER, PAUL BARKAN,[2] AINO LUSI[2] AND HELMUT RINGSDORF[2]

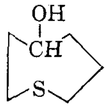
RECEIVED JANUARY 5, 1962

Dieckmann ring closure on the appropriate sulfide diesters under high dilution conditions resulted in the formation of 1-thiacycloöctane-5-one and 1-thiacyclononane-5-one. An investigation of these medium-sized ring ketosulfides disclosed sulfur–carbon ring closure in the eight- and nine-membered ring compounds. The bicyclic perchlorate salts were formed by transannular reactions.

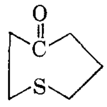
In the course of our investigations of cyclic sulfones of type I[3] several sulfur-containing ring compounds were prepared (II, III, IV, V).[4–6] In this paper we want to report the preparation and reactions of eight- and nine-membered cyclic sulfides.



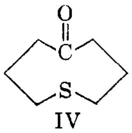
I



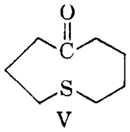
II



III



IV



V

The eight-membered ring ketosulfide IV, 1-thiacycloöctane-5-one, was prepared by the Dieckmann cyclization of diethyl γ,γ'-thiabis-*n*-butyrate (VI) under high dilution conditions, followed by hydrolysis and decarboxylation of the intermediate β-ketoester VII. The infrared spectrum of the eight-membered ring ketone IV in carbon tetrachloride showed a strong normal carbonyl absorption at 1705 cm.$^{-1}$, but in addition there was a shoulder at 1695 cm.$^{-1}$ (Table I). We have reported previously a single absorption for the seven-membered ring homolog III[3] at 1711 cm.$^{-1}$. The carbonyl doublet for the eight-membered ring was

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[1] This is the 8th in a series of papers concerned with the chemistry of cyclic sulfides and sulfones. For the previous paper in this series, see C. G. Overberger and J. M. Whelan, *J. Org. Chem.*, **26**, 4328 (1961). A preliminary account of this work was reported in an earlier communication.[4]

[2] This paper comprises parts of the dissertations submitted by Paul Barkan and Aino Lusi in partial fulfillment of the requirements for the degree of Master of Science in the Graduate School of the Polytechnic Institute of Brooklyn. Helmut Ringsdorf, present address: Institut Für Polymere, Universität Marburg, Germany.

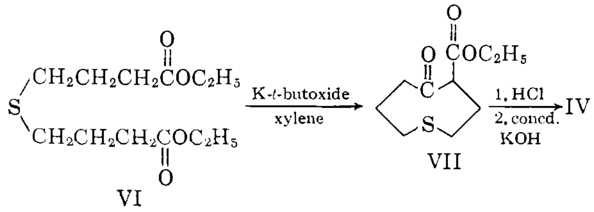
[3] C. G. Overberger and A. Katchman, *J. Am. Chem. Soc.*, **78**, 1965 (1956).

[4] C. G. Overberger and A. Lusi, *ibid.*, **81**, 506 (1959).

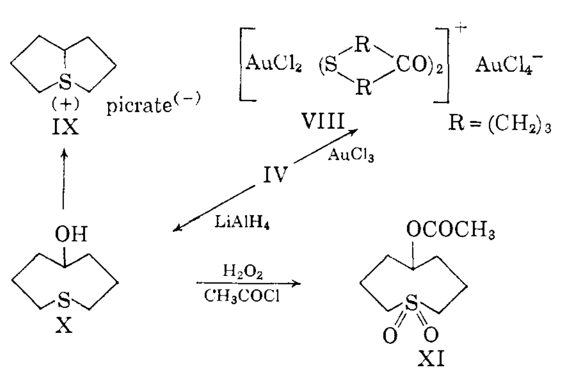
[5] N. J. Leonard, T. L. Brown and T. W. Milligan, *ibid.*, **81**, 507 (1959).

[6] N. J. Leonard, T. W. Milligan and T. L. Brown, *ibid.*, **82**, 4075 (1960).

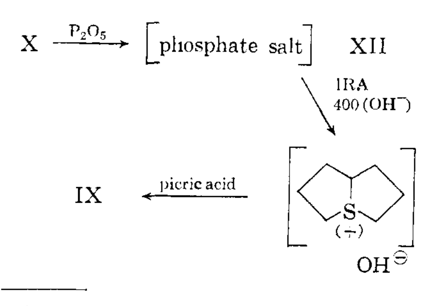
also reported by reference 5 and is similar to what has been observed in the nitrogen systems.[7]



1-Thiacyclooctane-5-one (IV) was reduced to give 5-hydroxy-1-thiacyclooctane (X) by reaction with lithium aluminum hydride. The alcohol was characterized by its acetyl and *m*-nitrobenzenesulfonate derivatives. Oxidation of 5-hydroxy-1-thiacyclooctane (X) in glacial acetic acid with 30% hydrogen peroxide followed by acetylation with acetyl chloride gave 5-acetoxy-1-thiacyclooctane-1,1-dioxide (XI).



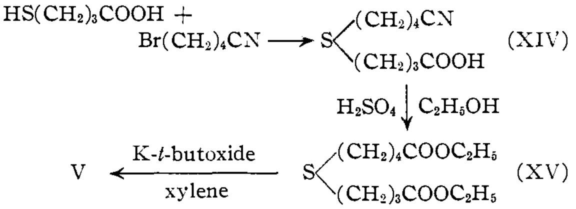
A series of unsuccessful attempts was made to prepare $\Delta^{4,5}$-1-thiacyclooctane by dehydration of the alcohol X or pyrolysis of its acetate. When phosphoric anhydride was used as the dehydration agent, a salt (XII) was formed. This intermediate was not isolated but deionization of the aqueous solution with IRA 400 on an OH^- cycle and reaction of the sulfonium hydroxide with picric acid gave bicyclo[3,3.0]octane-1-thianium picrate (IX). This sulfonium picrate was identical with the same compound reported by R. H. Eastman and G. Kritschevsky by an independent synthesis.[8]



The reaction to form the sulfonium salt may proceed by displacement of the sulfur atom on an intermediate phosphate ester or on an intermediate oxonium salt (conjugate acid of X). Both mechanisms have been discussed in the literature for the formation of sulfonium salts using mixtures of alcohols and sulfuric acid,[9,10] *p*-toluenesulfonic acid[11] and perchloric acid.[12] Meerwein[13] has demonstrated the preparation of sulfonium salts by reaction of thioethers with oxonium salts. We are currently investigating this reaction to see if it will apply to simple ring closures.

Reaction of 1-thiacyclooctane-5-one (IV) with perchloric acid gave a bicyclic hydroxy perchlorate. This compound has been recently described by Leonard and co-workers.[6] Attempts to prepare other bicyclic salts of this type by transannular reaction of the ketone IV with sulfonic and chlorosulfonic acid gave salts which showed transparency in the carbonyl region on infrared analysis but could not be characterized. The reaction of 1-thiacyclooctane-5-one (IV) with chloroauric acid yielded yellow crystals. An infrared absorption spectrum showed a carbonyl band at 1684 cm.⁻¹, indicating that salt formation had not taken place. On the basis of analysis and the infrared spectrum a coordination complex (VIII) between the cyclic ketosulfide and gold trichloride is suggested. This is in agreement with other reported complexes of linear and cyclic ketosulfides.[14,15]

For the synthesis of the 9-membered ring ketosulfide V, ω-carboethoxypropyl ω′-carboethoxybutyl sulfide XV was prepared in 31% yield by the reaction of γ-mercaptobutyric acid with 5-bromovaleronitrile, followed by esterification of the intermediate sulfide acid-nitrile XIV. The Dieckmann ring closure of the unsymmetrical sulfide diester XV, using xylene as solvent and potassium *t*-butoxide as the base for the condensation, yielded 1-thiacyclononane-5-one (V).



$$\mathrm{HS(CH_2)_3COOH} + \mathrm{Br(CH_2)_4CN} \longrightarrow \mathrm{S}\begin{cases}\mathrm{(CH_2)_4CN}\\ \mathrm{(CH_2)_3COOH}\end{cases} \quad \text{(XIV)}$$

$$\Big\downarrow \mathrm{H_2SO_4}\ \mathrm{C_2H_5OH}$$

$$\mathrm{V} \xleftarrow[\text{xylene}]{\text{K-}t\text{-butoxide}} \mathrm{S}\begin{cases}\mathrm{(CH_2)_4COOC_2H_5}\\ \mathrm{(CH_2)_3COOC_2H_5}\end{cases} \quad \text{(XV)}$$

The infrared spectrum of the nine-membered ring ketosulfide V in carbon tetrachloride showed a normal carbonyl band at 1708 cm.⁻¹ and no shoulder (Table I). 1-Thiacyclononane-5-one (V) was characterized by a transannular reaction with a perchloric acid ether solution to form 5-hydroxybicyclo[4,3,0]nonane - 1 - thianium perchlorate (XVI). The reaction with perchloric acid probably involves protonation of the carbonyl oxygen

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[7] N. J. Leonard, M. Oki, J. Brader and H. Boaz, *J. Am. Chem. Soc.*, **77**, 6237 (1955), and earlier papers.

[8] We are indebted to Dr. R. Eastman and Dr. G. Kritschevsky for a sample of this picrate. Their compound was prepared by the conversion of 3-(2-tetrahydrofuryl)-propyl chloride into its isothiuronium salt. Treatment of the latter with ammonium hydroxide yielded the mercaptan which gave bicyclo[3.3.0]octane-1-thianium chloride when allowed to react with concentrated hydrochloric acid at 100°. Isolation was then carried out by the formation of the picrate (*J. Org. Chem.*, **24**, 1428 (1959)).

[9] F. E. Ray and J. L. Farmer, *J. Org. Chem.*, **8**, 391 (1943).

[10] T. F. Lavine, N. F. Floyd and M. S. Cammaroti, *J. Biol. Chem.*, **207**, 107 (1954).

[11] A. J. Van Peski and J. M. Hoesselman, Holland Patent 47715, 47897 (1937).

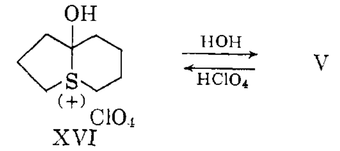
[12] O. Hinsberg, *Ber.*, **69**, 492 (1936).

[13] H. Meerwein, G. Hinz, P. Hofmann, E. Kroning and E. Pfeil, *J. prakt. Chem.*, [2] **147**, 257 (1937).

[14] G. M. Bennett and L. V. D. Scorah, *J. Chem. Soc.*, 194 (1927).

[15] "Methoden der Org. Chemie," edited by E. Müller, Band II, Georg Thieme, Verlag Stuttgart, 1953, p. 588.

followed by reaction with the ring sulfur which is held in close proximity.

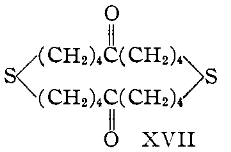


XVI

The bicyclic perchlorate salt XVI showed OH-absorption in the infrared at 3340 cm.$^{-1}$ but was transparent in the carbonyl region. It dissociates in water to give the free ketone V.

An attempt to prepare the nine-membered ring ketone through the acyloin condensation of diethyl γ,γ'-thia-bis-*n*-butyrate gave a hydroxy ketone which was then reduced with zinc dust and glacial acetic acid. The crude ketone was treated with perchloric acid to yield a crystalline solid, believed to be XVI, but which could not be characterized.

An attempt to prepare a 10-membered ring ketone by the Dieckmann ring closure of diethyl ω,ω'-thia-bis-valerate resulted in the formation of the 20-membered ring compound 1,11-dithiacycloeicosane-6,16-dione (XVII). The sixteen-membered ring ketosulfide has been reported to be a by-product in the synthesis of 1-thiacycloöctan-5-one.[6]



XVII

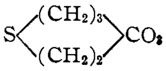
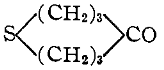
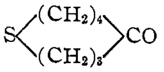
The infrared spectrum of the 20-membered ring diketone disulfide (XVII) showed a normal carbonyl band at 1710 cm.$^{-1}$. The compound did not undergo a transannular reaction with perchloric acid.

Thus it is clear that transannular ring closures in cyclic sulfur-containing compounds are influenced by the ability of the ring system to assume a stable conformation in which the sulfur and the reactive group are in close enough proximity for reaction to occur. These stable conformations correspond to the structure of a bicyclic product.

Table I summarizes infrared spectral data for cyclic ketosulfides.

Table I

Carbonyl Absorptions of Cyclic Ketosulfides

Ring size	Compound		λ_{max}, cm.$^{-1}$ In CCl_4	In $CHCl_3$
	CH_3COCH_3[17]		1719	1712
	$CH_3S(CH_2)_3COCH_3$[6]		1720	1710
6	$(CH_2)_5CO$[17]		1719	1705
7	 $S\begin{matrix}\diagup(CH_2)_3\diagdown\\ \diagdown(CH_2)_2\diagup\end{matrix}CO$[3]		1711	..
8	 $S\begin{matrix}\diagup(CH_2)_3\diagdown\\ \diagdown(CH_2)_3\diagup\end{matrix}CO$	Main band Shoulder	1705 1695	1685 1695
9	 $S\begin{matrix}\diagup(CH_2)_4\diagdown\\ \diagdown(CH_2)_3\diagup\end{matrix}CO$	Main band Shoulder	1708 None	1694 1705
20	1,11-Dithiacycloeicosane-6,16-dione		..	1710

It was surmised earlier that modifications of the carbonyl band in the infrared spectrum of medium-sized cyclic ketosulfides suggested the existence of mixtures of interacted and non-interacted conformations.[3–6] Later unpublished work by Leonard and co-workers[16] has indicated that carbonyl frequency fluctuation and carbonyl splitting may not be a direct result of conformational interaction but rather may be due to Fermi resonance and (or) combination bands in the infrared.

Experimental[18]

Diethyl γ,γ'-Thia-bis-butyrate (VI).—Following the procedure of Overberger and Tashlick,[19] anhydrous alcohol (320 ml.) was treated with 17.9 g. (0.78 g.-atm.) of sodium metal under anhydrous conditions.[19] When reaction was complete, hydrogen sulfide was bubbled into the solution for 8 hours, and then a second solution of 17.9 g. of sodium in 320 ml. of ethanol was added and the solution refluxed for 2 hours. Then 300 g. (1.54 moles) of ethyl γ-bromobutyrate (b.p. 79–81° (9 mm.)) was added dropwise with stirring over 45 minutes, the reaction mixture becoming warm and sodium bromide precipitating. After the reaction mixture was refluxed with stirring for 5 hours, 500 ml. of ethanol was distilled and 625 ml. of cold water added to the residue. An organic layer separated and the sodium bromide dissolved. Layers were separated and the aqueous layer was extracted with ether. The organic layer and the ether extracts were combined and dried over anhydrous magnesium sulfate. The ether was distilled and the residue fractionated to yield a colorless liquid, b.p. 124–126° (0.7 mm.), 130 g. (64.3%).

Anal. Calcd. for $C_{12}H_{22}O_4S$: C, 54.91; H, 8.45; S, 12.22. Found: C, 54.95; H, 8.51; S, 11.87.

1-Thiacycloöctane-5-one (IV).—A 3-necked, 1-liter reaction flask was equipped with a high speed stirrer, an inlet tube for the introduction of nitrogen gas, and the third neck connected to a cyclic high dilution apparatus.[20] The reaction flask and high dilution apparatus were wrapped with asbestos rope. A continuous flow of nitrogen, purified by passage through two wash bottles of Fieser solution, one of concentrated sulfuric acid and drying tower of anhydrous barium oxide, was maintained throughout the reaction.

Freshly cleaned potassium metal was weighed in a beaker of dry xylene, and then transferred into a known volume of excess *t*-butyl alcohol, which had been previously distilled from sodium. After all the potassium had reacted, the solution was allowed to cool and an 85-ml. aliquot of potassium *t*-butoxide (0.12 mole) in *t*-butyl alcohol was transferred into the reaction flask. To this, 300 ml. of xylene, dried over sodium wire and distilled immediately before use, was added. The reaction mixture was heated, a stopcock opened for the removal of the alcohol–xylene azeotrope, and distillation continued until the temperature of the distilling vapors had risen to 135°. The stopcock was closed and enough xylene added to bring the total volume in the flask to 400 ml. Then 15.0 g. (0.057 mole) of diethyl γ,γ'-thia-bis-butyrate (VI) in 150 ml. of dry xylene was added dropwise to the reaction mixture *via* a Hershberg funnel during 55 hours, with vigorous stirring and strong reflux. Alcohol formed during the reaction was periodically removed by opening the stopcock, the total volume being maintained at about 400 ml. After completion of the addition, the mixture was allowed to cool overnight under nitrogen with slow stirring. The orange-brown reaction mixture was extracted with three 100-ml. volumes of 2.5 *N* hydrochloric acid, three times with 100 ml. of 5% aqueous sodium bicarbonate, and washed twice with water. The

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[16] Private communication by N. J. Leonard, University of Illinois, Urbana, Ill.

[17] L. J. Bellamy and R. L. Williams, *Trans. Faraday Soc.*, **55**, 15 (1959).

[18] Microanalysis by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y., and A. Bernhardt, Mikroanalytisches Laboratorium, Muehlheim/Ruhr, West-Germany. Melting points and boiling points are uncorrected.

[19] I. Tashlick, M. S. Thesis, Polytechnic Institute of Brooklyn, June, 1953.

[20] N. J. Leonard and R. C. Sentz, *J. Am. Chem. Soc.*, **74**, 1704 (1952).

xylene layer was dried over anhydrous magnesium sulfate, the solvent removed, and the orange colored oil hydrolyzed by refluxing for 2.5 hours with a mixture of 70 ml. of concentrated and 120 ml. of 2.5 *N* hydrochloric acid. The hydrolysate was cooled below 5° in an ice-bath and made strongly alkaline by the addition of a cold saturated potassium hydroxide solution in small portions, keeping the temperature as close to 5° as possible. It was immediately extracted with ether. After drying the ether solution and removing the solvent, distillation of the residue gave a colorless liquid, b.p. 120–123° (19 mm.), 1.9 g. (23%), which crystallized in the receiver. Recrystallization of the product from an ether–petroleum ether solution gave white needle crystals, m.p. 50–52°. The compound exhibited strong infrared absorption for the carbonyl group (—C═O at 1690 cm.$^{-1}$, with a shoulder at 1705 cm.$^{-1}$, in KBr). In carbon tetrachloride, there was a peak at 1705 cm.$^{-1}$ with a shoulder at 1695 cm.$^{-1}$, and in chloroform there was a peak at 1685 cm.$^{-1}$ with a shoulder at 1695 cm.$^{-1}$ (2.5% soln.).

Anal. Calcd. for $C_7H_{12}OS$: C, 58.29; H, 8.39. Found: C, 58.26; H, 8.39.

A 2,4-dinitrophenylhydrazone derivative of the 8-membered ring ketosulfide IV was prepared in an ethanol-sulfuric acid solution. The compound was recrystallized from ethanol; m.p. 194–195°. A mixed melting point of the derivative with the reagent 2,4-dinitrophenylhydrazine, m.p. 194–197°, was depressed, m.p. 167–187°. The derivative was insoluble in 2.5 *N* hydrochloric acid, and a sodium fusion resulted in a strong positive test for sulfide ion.

Anal. Calcd. for $C_{13}H_{16}N_4OS$: N, 17.25. Found: N, 17.34.

5-Hydroxy-1-thiacycloöctane (X).—1-Thiacycloöctane-5-one (IV) (2.0 g., 0.014 mole) in 53 ml. of anhydrous ether was added dropwise to a stirred suspension of 0.34 g. (0.008 mole) of lithium aluminum hydride in 53 ml. of absolute ethyl ether. After the addition was completed, the reaction mixture was refluxed for 1 hour. Sufficient 7.5% sulfuric acid was added to dissolve all solids followed by 53 ml. of water. The solution was extracted with six 50-ml. portions of ether. The ether solution was dried over anhydrous magnesium sulfate, the ether removed, and the residue distilled to yield a colorless, viscous liquid, b.p. 73–75° (1.5 mm.), 1.2 g. (60.0%), $n^{25}\text{D}$ 1.5388, which solidified in the receiver. The product was redistilled to give a colorless liquid, which crystallized to form needle crystals, m.p. 25.6–26.3°. The infrared absorption spectrum of the compound showed strong hydroxyl absorption at 3380 cm.$^{-1}$, and no carbonyl absorption.

Anal. Calcd. for $C_7H_{14}OS$: C, 57.48; H, 9.66. Found: C, 57.36; H, 9.75.

5-Thiacycloöctanyl *m*-Nitrobenzenesulfonate.—The carbinol X (50 mg., 0.00034 mole) was dissolved in benzene, slightly less than one equivalent of *m*-nitrobenzenesulfonyl chloride was added and the solution was refluxed for 1 hour. The solvent was removed and the ester crystallized twice from chloroform and a few drops of ethyl ether; 55 mg. (73%), m.p. 108–110°.

Anal. Calcd. for $C_{13}H_{17}NO_5S_2$: C, 47.11; H, 5.17. Found: C, 46.97; H, 5.34.

5-Acetoxy-1-thiacycloöctane 1,1-Dioxide (XI).—A procedure described by Overberger and Katchman[3] for a seven-membered ring analog was used. To a solution of 0.28 g. (0.002 mole) of 5-hydroxy-1-thiacycloöctane (X) in 3 ml. of glacial acetic acid, 0.65 ml. (0.0057 mole) of 30% hydrogen peroxide was added in small portions, with slight cooling. The mixture was allowed to stand at room temperature overnight and the reaction mixture was then heated to decompose the excess peroxide. The solvent was removed under reduced pressure and the residue was refluxed for 1 hour with an excess of acetyl chloride. The acid chloride was then distilled and the residue was recrystallized four times from isopropyl alcohol to which had been added some petroleum ether; m.p. 70–71°, 0.25 g. (57%).

Anal. Calcd. for $C_9H_{16}O_4S$: C, 49.06; H, 7.32; S, 14.56. Found: C, 49.12; H, 7.35; S, 14.49.

Bicyclo[3,3,0]octane-1-thianium Picrate (IX).—5-Hydroxy-1-thiacycloöctane (X) (1.0 g., 0.007 mole) was refluxed with 1.5 g. of phosphorus pentoxide in 100 ml. of benzene for 5 hours. The solvent layer was decanted from the phosphoric acid residue and the solvent removed under reduced pressure. The very small amount of residue so obtained did not give the usual tests for an olefinic compound. The phosphoric acid residue was now dissolved in 80 ml. of water and neutralized with Amberlite IRA 400 anion exchange resin on OH-cycle. The solution was filtered and to about 20 ml. half as much aqueous saturated picric acid solution was added. On standing, yellow crystals precipitated, 74.7 mg; recrystallization from ethanol gave a m.p. 262–264° dec.

Anal. Calcd. for $C_{13}H_{15}N_3O_7S$: C, 43.75; H, 4.22; N, 11.78. Found: C, 43.55; H, 4.23; N, 11.75.

This sulfonium picrate was identical (infrared spectrum) with the same compound reported by R. H. Eastman and G. Kritschevsky,[8] m.p. 261–263°, mixed m.p. 261–264°.

Dichloro-bis-(1-thiacycloöctane-5-one)-gold(III) Tetrachloroaurate(III) (VIII).—A dilute solution of $HAuCl_4 \cdot 3H_2O$ in ethyl ether was added dropwise to a solution of 1-thiacycloöctane-5-one (IV) in ether until precipitation was complete. The yellow solid which formed was recrystallized from an ether–acetone solution to give a yellow crystalline solid, m.p. 99–101°. The infrared absorption spectrum of the compound showed a carbonyl peak at 1684 cm.$^{-1}$ (KBr), indicating that salt formation had not occurred. The solid was unstable in the presence of light and decomposed on standing, changing from yellow to red to black in color.

Anal. Calcd. for $C_{14}H_{24}Au_2Cl_6O_2S_2$: C, 21.05; H, 3.13. Found: C, 20.81; H, 3.27.

γ-Mercaptobutyric Acid.—Employing a general method described in reference 21, a solution of 80.0 g. (0.5 mole) of potassium ethyl xanthate in 600 ml. of methanol was added at once to a solution of 100.0 g. (0.5 mole) of ethyl γ-bromobutyrate (b.p. 79–81° (9 mm.)) in 100 ml. of methanol. The mixture was allowed to react at room temperature for 24 hours with stirring, during which time it turned yellow-green in color and potassium bromide precipitated. In previous runs, when heat was applied the reaction took place at a faster rate but the yields of mercaptoacid were lower. Then, 600 ml. of methanol was removed under reduced pressure and the residue was hydrolyzed by heating overnight at 50° under nitrogen with a 20% potassium hydroxide solution. After cooling, the mixture was acidified to congo red with a 20% sulfuric acid solution, refluxed with zinc dust for 1 hour, and continuously extracted with ether for 24 hours. The ether solution was dried over anhydrous magnesium sulfate, the solvent removed, and the residue distilled to give a colorless liquid, b.p. 103–104° (2.6 mm.), 60.0 g. (97.5%), $n^{22}\text{D}$ 1.4935 ($n^{20}\text{D}$ 1.4912, by reaction of thioacetic acid and butenoic acid[22]).

ω-Carboethoxypropyl ω′-Carboethoxybutyl Sulfide (XV).—Anhydrous ethanol, 450 ml., was treated with 13.8 g. (0.60 g.-atm.) of sodium metal. After the reaction was completed, 46.0 g. (0.38 mole) of γ-mercaptobutyric acid was added dropwise over 15 minutes with rapid stirring under nitrogen. The di-sodium salt precipitated out of solution. To this slurry, 61.6 g. (0.38 mole) of 5-bromovaleronitrile (b.p. 110–112° (12 mm.)) was added dropwise with stirring over 1.5 hours. After allowing the mixture to react at room temperature for 24 hours, a solution of 3.5 g. (0.16 g.-atm.) of sodium in 60 ml. of ethanol was added to react with any remaining mercapto acid. The mixture was allowed to react at room temperature for an additional 24 hours and then was acidified with a dilute solution of sulfuric acid in ethanol. Ether was added, the precipitated sodium bromide was removed by filtration, and the volume of the filtrate was reduced to 200 ml. No attempt was made to isolate the sulfide acid-nitrile.

The ethanolic solution of the sulfide acid-nitrile was saponified by refluxing overnight with 35 ml. of concentrated sulfuric acid and 4 ml. of water. The sulfide di-acid formed was esterified by refluxing overnight with 50 ml. of ethanol and 150 ml. of benzene. After the azeotropic distillation of the water which formed and the removal of the solvents, the mixture was poured into ice-water and an organic layer separated. The aqueous layer was extracted with ether and the combined organic layer and ether extracts were washed successively with a 5% sodium bicarbonate solution

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(21) "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 363.

(22) B. Holmberg and E. Schjanberg, *Arch. Kemi, Mineral., Geol.*, **14A**, 22 (1940).

and water. The ether solution was dried over anhydrous magnesium sulfate, the solvent removed, and the residue distilled to give a colorless liquid, b.p. 129–131° (0.15 mm.), 33.0 g. (31.2%), $n^{25}\text{D}$ 1.4675. The infrared absorption spectrum of the compound showed a carbonyl peak at 1740 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{24}O_4S$: C, 56.49; H, 8.75; S, 11.60. Found: C, 56.03; H, 8.78; S, 11.90.

1-Thiacyclononane-5-one (V).—The procedure employed for the synthesis of the nine-membered ring ketosulfide was similar to that used for the preparation of 1-thiacycloöctane-5-one (IV). The apparatus which was used consisted of a 1-liter Morton flask equipped with a high speed stirrer, a cyclic high dilution apparatus and a Hershberg addition funnel. A continuous stream of nitrogen gas, purified by passage through two wash bottles containing the metal ketyl from benzophenone and sodium and one of glass wool, was passed through the apparatus throughout the reaction.

Into the reaction flask was placed 400 ml. of xylene and 60 ml. of *t*-butyl alcohol, both previously distilled from sodium, and 5.1 g. (0.130 g.-at.) of potassium metal. The mixture was stirred and warmed gently until all the potassium had reacted, and then the excess alcohol was distilled until the temperature of the distillate reached 134°. The volume was adjusted to about 400 ml. by the addition of xylene, and a solution of 20.0 g. (0.072 mole) of ω-carboethoxypropyl ω′-carboethoxybutyl sulfide (XV) in 250 ml. of dry xylene was added through the Hershberg funnel over 52 hours under a continuous stream of nitrogen, with vigorous reflux and high speed stirring. The volume was maintained approximately constant by the periodic addition of xylene and removal of ethanol by distillation. The mixture was heated and stirred for a further 1.5 hours, cooled to room temperature, and washed successively with 2.5 *N* hydrochloric acid, 5% aqueous sodium bicarbonate, and water. The xylene was removed by evaporation at reduced pressure, leaving a residual orange oil which was refluxed for 3 hours with 100 ml. of 6 *N* hydrochloric acid to effect hydrolysis and decarboxylation. The acid solution was cooled to 5° and was maintained below 15° while being made strongly alkaline by the slow addition of a saturated potassium hydroxide solution. The cold yellow basic solution was extracted immediately with ether. The ethereal solution was dried, concentrated at reduced pressure, and the residue distilled through a molecular still to give a few milliliters of a viscous yellow liquid. An infrared absorption spectrum showed carbonyl peaks at 1740 and 1705 cm.$^{-1}$. The impure liquid was treated with a perchloric acid–ether solution to yield a crystalline perchlorate salt. This salt was decomposed with 5% aqueous sodium hydroxide and the mixture extracted with ether. Removal of the solvent yielded about 100 mg. of a colorless liquid which crystallized in an ice-bath, but which liquefied as the temperature was raised. The compound was characterized by its infrared absorption spectra in carbon tetrachloride (—C=O at 1708 cm.$^{-1}$) and in chloroform (—C=O at 1694 cm.$^{-1}$ with a shoulder at 1705 cm.$^{-1}$), and by analysis.

Anal. Calcd. for $C_8H_{14}OS$: C, 60.71; H, 8.92. Found: C, 60.60; H, 8.99.

In addition, the reaction mixture yielded a polymeric material, some unreacted starting material and 10.3 g. (64.3%), of the unsymmetrical sulfide di-acid, ω-carboxypropyl ω′-carboxybutyl sulfide, which was recrystallized from benzene, m.p. 85–86°.

Anal. Calcd. for $C_9H_{16}O_4S$: C, 49.03; H, 7.32; S, 14.56. Found: C, 49.17; H, 7.27; S, 14.70.

5-Hydroxybicyclo[4.3.0]nonane-1-thianium Perchlorate (XVI).—An ether solution of 1-thiacyclononane-5-one (V) was treated with a perchloric acid–ether solution to yield 180 mg. of a white crystalline precipitate. This was recrystallized from a benzene–ether solution to give a crystalline solid, m.p. 160–162° dec. An infrared absorption spectrum of the salt showed an -OH peak at 3340 cm.$^{-1}$ and transparency in the 6 μ region (Nujol mull).

Anal. Calcd. for $C_8H_{15}ClO_5S$: C, 37.14; H, 5.84; Cl, 13.70; S, 12.39. Found: C, 37.35; H, 5.91; Cl, 13.56; S, 12.69.

Diethyl ω,ω′-Thia-bis-valerate.—Following a method similar to that used for the preparation of VI, anhydrous alcohol, 132 ml., was treated with 7.36 g. (0.32 g.-at.) of sodium metal under anhydrous conditions. After the reaction was completed, hydrogen sulfide was bubbled into the solution for 7 hours. When the solution was saturated with the gas, a second solution of 7.36 g. of sodium in 132 ml. of ethanol was added and the mixture refluxed on a steam-bath for 2 hours. Then 100.0 g. (0.62 mole) of 5-bromovaleronitrile was added dropwise with stirring over 30 minutes. The reaction mixture became warm and a precipitate of sodium bromide formed. The mixture was refluxed with stirring for 4 hours; 200 ml. of ethanol was distilled and 100 ml. of cold water added to the residue. An organic layer separated and the sodium bromide dissolved. Layers were separated, the aqueous layer was extracted with four 100-ml. portions of ether, and the organic layer and ether extracts combined and dried over anhydrous sodium sulfate. The ether was removed, leaving an orange-red liquid.

The sulfide di-nitrile was esterified by refluxing overnight with 300 ml. of absolute ethanol, 111 ml. of concentrated sulfuric acid and 22 ml. of water. The mixture was poured into ice-water, an organic layer separating. The aqueous layer was extracted with ether and the combined organic layer and ether extracts washed successively with 5% aqueous sodium bicarbonate, and water, and dried over anhydrous magnesium sulfate. The ether was removed and the residue distilled to yield a pale yellow liquid, b.p. 137–139° (0.12 mm.), 19.9 g. (21.2%), $n^{26}\text{D}$ 1.4688.

Anal. Calcd. for $C_{14}H_{26}O_4S$: C, 57.93; H, 8.97; S, 11.04. Found: C, 57.69; H, 9.04; S, 11.23.

Attempt to Prepare 1-Thiacyclodecane-6-one.—The procedure and apparatus used for the synthesis of the ten-membered ring ketosulfide was identical with that employed for the preparation of 1-thiacyclononane-5-one (V).

Into the reaction flask was placed 400 ml. of xylene and 42 ml. of *t*-butyl alcohol, both previously distilled from sodium, and 3.9 g. (0.10 g.-atm.) of potassium metal. The mixture was stirred and warmed gently until all the potassium had reacted, and then the excess alcohol was distilled until the temperature of the distillate reached 134°. The volume was adjusted to about 400 ml. by the addition of xylene, and then a solution of 15.0 g. (0.052 mole) of ethyl thio-di-*n*-valerate (XIX) in 350 ml. of dry xylene was added over 50 hours. The mixture was heated and stirred for an additional hour, cooled to room temperature, and washed successively with 2.5 *N* hydrochloric acid, 5% aqueous sodium bicarbonate, and water. The xylene was removed and the residual orange oil refluxed for 3 hours with 95 ml. of 6 *N* hydrochloric acid to effect hydrolysis and decarboxylation. The acid solution was cooled to 5° and was maintained below 15° while being made strongly basic by the slow addition of a saturated potassium hydroxide solution. The yellow alkaline solution was extracted immediately with ether. The ethereal solution was dried, concentrated at reduced pressure, and the residue distilled to give a viscous orange oil. On standing, a solid separated from the oil. This was recrystallized from heptane to yield white needle crystals, m.p. 112.5–113.5°. An infrared absorption spectrum of the solid showed two carbonyl peaks of almost equal intensity (1740 and 1710 cm.$^{-1}$, KBr). Analysis indicated that the compound was either a linear condensation product, or the cyclic β-ketoester. The solid was treated with a dilute potassium hydroxide solution and heated at 110° in an oil-bath for 3 days. The mixture was extracted with ether, and the ether evaporated to yield 15 mg. of a white solid, whose infrared spectrum showed a single carbonyl peak at 1705 cm.$^{-1}$, KBr (1710 cm.$^{-1}$ in chloroform). The solid was recrystallized from heptane to give white needle crystals, m.p. 53–54°. The compound did not react with a perchloric acid–ether solution. Analysis indicated that the compound was the twenty-membered ring ketosulfide, 1,11-dithiacycloeicosane-6,16-dione (XVII).

Anal. Calcd. for $C_{18}H_{32}O_2S_2$: C, 62.74; H, 9.36; mol. wt., 344. Found: C, 62.81; H, 9.37; mol. wt. (Rast), 303.

In addition, the reaction mixture yielded some unreacted starting material, and 5.0 g. (43.2%) of the symmetrical sulfide di-acid, δ,δ′-thio-di-valeric acid. This was recrystallized from benzene to yield a white crystalline solid, m.p. 96.5–97.5°.[23]

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[23] A. N. Nesmejanow, *et. al.*, *Chem. Tech.* (*Berlin*), **9**, 139 (1957)